The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte TERRY B. STROM, XIN X. ZHENG and ALAN STEELE

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Appeal No. 2000-0839[1]
Application No. 08/355,502

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HEARD: November 29, 2001

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Before WILLIAM F. SMITH, SCHEINER and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-4 and 8-10, which are all the claims pending in the application.

[1] We note that this appeal is related to Appeal No. 2001-0893 (Application No. 08/968,905) accordingly these two appeals were considered together.

Claims 1 and 3 are illustrative of the subject matter on appeal and are reproduced below:

1. A chimeric protein comprising a mature IL-10 bonded to a polypeptide, said polypeptide comprising the Fc region of IgG, said Fc region of IgG having a circulating half-life by itself which is greater than that of IL-10.

3. The chimeric protein of claim 2 wherein said Fc region includes a mutation which inhibits complement fixation and Fc receptor binding by said protein, said mutation being a substitution mutation replacing at least one of the amino acids selected from the group consisting of Leu 235, Glu 318, Lys 320, and Lys 322 found in the murine CH2 domain.

The references relied upon by the examiner are:

Capon et al. (Capon)	5,116,964	May. 26, 1992
Mosmann et al. (Mosmann)	5,231,012	Jul. 27, 1993
Winter et al. (Winter)	WO 88/07089	Mar. 18, 1988

Appellants rely on:

Capon et al. (Capon II), "Designing CD4 immunoadhesins for AIDS therapy," Nature, Vol. 337, pp. 525-531 (1989)

GROUNDS OF REJECTION

Claims 1, 2, 4 and 8-10 stand rejected under 35 U.S.C. § 103 as being unpatentable over Capon in view of Mosmann.

Claim 3 stands rejected under 35 U.S.C. § 103 as being unpatentable over Capon in view of Mosmann and further in view of Winter.

We reverse.

DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer[2] for the examiner's reasoning in support of the rejections. We further reference appellants' Brief[3], and Reply Brief[4] for the appellants' arguments in favor of patentability. We note the examiner entered and considered appellants' Reply Brief.[5]

THE REJECTIONS UNDER 35 U.S.C. § 103:

Claims 1, 2, 4 and 8-10:

According to the examiner (Answer, page 4) Capon teach:

> chimeric proteins for directing ligand binding partners such as growth factors, hormones or effector molecules to cells bearing ligands for the ligand binding partners comprising a ligand binding partners fused to a stable plasma protein which is capable of extending the in vivo half-life of the loigand binding partner when present as a fusion with the ligand binding partner, in particular wherein such a stable plasma protein is an immunoglobulin constant domain.

While the examiner does not expressly recognize this fact, Capon does not teach IL-10. The examiner applies Mosmann to make up for this deficiency in Capon. According to the examiner (Answer, bridging paragraph, pages 4-5)

[2] Paper No. 26, mailed October 14, 1999.
[3] Paper No. 25, received September 14, 1999.
[4] Paper No. 28, received December 6, 1999.
[5] Paper No. 29, mailed February 22, 2000.

Mosmann teach "the nucleotide and corresponding amino acid sequence of mammalian IL-10, a method for producing the IL-10 polypeptide and the IL-10 peptide in a pharmaceutically acceptable carrier, but does not teach chimeric proteins comprising IL-10 bonded to the Fc region of an IgG molecule which increases it[s] circulating half-life." The examiner finds (Answer, page 5) that "[o]ne would have been motivated to use a chimeric protein comprising IL-10 and Fc to decrease its clearance rate in vivo…."

In response, appellants direct our attention to Capon II arguing (Brief, page 7) that Capon II:

> reported fusion between CD4 and the Fc region of IgG…. Capon [II] expected both portions of the molecule to retain their biological activities after the fusion because CD4 contains immunoglobulin-like domains that are highly reminiscent of the domains in the immunoglobulin molecule itself. However, despite this sound reasoning, Capon [II] discovered that the CD4/Fc chimera did NOT retain all of the biological properties of its Fc component. Accordingly, one of ordinary skill in the art, viewing the art as a whole, would learn that even when the characteristics of two molecules suggest that they will fold in a compatible way, biological activity can be lost.

According to appellants (Brief, page 6) "[t]he [e]xaminer has disregarded this argument … simply because it is based in part on a reference that was initially applied against the claims and then withdrawn." We note the examiner's statement (Answer, page 10) "[w]ith respect to [a]pplicants arguments concerning … [Capon II], the instant rejection is based on the subsequent Capon et al. '964 patent which is presently being applied to the claims." It is not sufficient for the examiner to dismiss appellants' evidence of non-obviousness, simply because the reference supporting

appellants' argument is no longer relied on by the examiner. As set forth In re Rinehart, 531 F.2d 1048, 1052, 189 UPSQ 143, 147 (CCPA 1976):

> When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over. … An earlier decision should not, as it was here, be considered as set in concrete, and applicant's rebuttal evidence then be evaluated only on its knockdown ability. Analytical fixation on an earlier decision can tend to provide that decision with an undeservedly broadened umbrella effect. Prima facie obviousness is a legal conclusion, not a fact. Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, not against the conclusion itself. … [A] final finding of obviousness may of course be reached, but such finding will rest upon evaluation of all facts in evidence, uninfluenced by any earlier conclusion reached by an earlier board upon a different record.

To the extent that the examiner relies on some additional teaching in the '964 patent to overcome the teaching away in Capon II, the examiner fails to elucidate this additional teaching on this record. We remind the examiner that in order to establish a prima facie case of obviousness, there must be both, a suggestion or motivation to modify the references or combine reference teachings, and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). While it may be "obvious to try" the general approach set forth in the '964 patent, to produce an IL-10/Fc fusion; obvious to try is not the standard of obviousness. In re O'Farrell, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). In our opinion, based on the evidence of record in this application, a person of ordinary skill in the art would not have had a reasonable expectation of success in obtaining a IL-10/Fc fusion wherein both ends retain their biological activity.

We are not persuaded by the examiner's argument (Answer, page 11) that "one of ordinary skill in the art would expect success with the IL-10/Fc chimera since claim 2 in the '964 patent expressly recites fusions of ligand binding partner proteins and immunoglobulin chains, and to expect otherwise one would have to consider the claim 2[6] of the '964 patent invalid." Instead, we agree with appellants' (Brief, page 13) that "Capon's claim 2 could be perfectly valid and yet not render obvious a species within it." In our opinion, this argument also attempts to improperly shift the examiner's burden[7] of establishing a prima facie case of obviousness to appellant.

On this record, appellants' provide evidence (Capon II) that a person of ordinary skill in the art would have had less than a reasonable expectation of success in obtaining an IL-10/Fc fusion protein wherein both ends retain their biological activity. Supporting this evidence, appellants argue (Brief, page 13) that while it is undisputed[8] that the scope of the '964 patent is immense, the patent also "fails to so much as mention the general class of molecules encompassing IL-10 …

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[6] Claim 2 ('964). Nucleic acid encoding a polypeptide fusion of a ligand binding partner protein and an immunoglobulin chain, wherein the ligand binding partner protein is not a platelet growth factor receptor or an insulin receptor said ligand binding partner protein and said immunoglobulin chain being fused through C- or N-terminal amino or carboxyl groups, and said fusion further comprising an additional fusion of an agent selected from the group consisting of a multiple subunit (chain) polypeptide, a portion or an immunoglobulin superfamily member, a toxin and a polypeptide therapeutic agent not otherwise associated with an immunoglobulin, and an immunoglobulin chain.

[7] It is the examiner who has the initial burden of presenting a prima facie case of obviousness. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

[8] The examiner agrees (Answer, page 8) that the scope of the '965 patent is immense.

[those molecules that are mentioned in the patent] fail to bear any structural or functional relationship to IL-10."

In response, the examiner argues (Answer, page 8) that the '964 patent demonstrates "that is was well known in the art at the time of the invention that production of a chimeric protein containing the Fc domain of IgG fused to any soluble protein would increase the circulating half-life of the protein." The examiner however, fails to identify any teaching in the art to support this position. We caution the examiner against the use of expansive generalizations. Instead, we remind the examiner that conclusions of obviousness must be based upon facts, not generality. In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968); In re Freed, 425 F.2d 785, 788, 165 USPQ 570, 571 (CCPA 1970). Here, the examiner offers no evidence to support her suggestion that the fusion of an IgG Fc domain to any soluble protein would necessarily increase its circulating half-life.

To the extent that the examiner would argue (Answer, page 9) that while the '964 patent does not teach IL-10, it does teach growth factors (column 7, lines 11-24), therefore since cytokines are growth factors, and IL-10 is a cytokine, the '964 patent includes IL-10, we can not agree. Instead, on this record, we agree with appellants (Brief, pages 10-11) there "is no suggestion that one should select a protein from … [the] vast number of possibilities [disclosed in the '964 patent] that has any particular structural or functional characteristics, let alone one having the characteristics of IL-10. Indeed, there is no mention of

either interleukins generally or IL-10 specifically." As set forth in Ecolochem Inc. v. Southern California Edison, 227, F.3d 1361, 1375, 56 USPQ2d 1065, 1075 (CAFC 2000) the:

> "[S]uggestion to combine may be found in explicit or implicit teachings within the references themselves, from the ordinary knowledge of those skilled in the art, or from the nature of the problem to be solved." … However, there still must be evidence that "a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." … "[A] rejection cannot be predicated on the mere identification … of individual components of claimed limitations. Rather particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."…. [Citations omitted].

On reflection, it is our opinion that the examiner failed to provide the evidence necessary to support a prima facie case of obviousness. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Accordingly, we reverse the rejection of claims 1, 2, 4 and 8-10 under 35 U.S.C. § 103 as being unpatentable over Capon in view of Mosmann.

Claim 3:

According to the examiner (Answer, page 6) the combination of Capon in view of Mosmann, discussed supra, does "not explicitly teach a chimeric protein comprising the Fc region of IgG which includes a mutation which is a substitution of [at] least one of the amino acids recited in claim 3." The examiner relies on Winter to teach the modification of conserved residues to abolish the abolish C1q binding

and thereby overcome the deficiency in the combination of Capon in view of Mosmann.

Winter, however, fails to make up for the deficiency in the underlying combination of Capon in view of Mosmann, as applied to claims 1, 2, 4 and 8-10, discussed supra. Thus, the examiner failed to establish the evidence necessary to maintain a prima facie case of obviousness. Accordingly, we reverse the rejection of claim 3 under 35 U.S.C. § 103 as being unpatentable over Capon in view of Mosmann and further in view of Winter.

REVERSED

William F. Smith	)
Administrative Patent Judge	)
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	)
	) BOARD OF PATENT
Toni R. Scheiner	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
Donald E. Adams	)
Administrative Patent Judge	)

DA/dym

Paul T. Clark
Fish & Richardson
225 Franklin Street
Boston, MA 02110-2804